

Applicability of the NASA Galactic Cosmic Ray Simulator for Large Animal Studies

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Outline

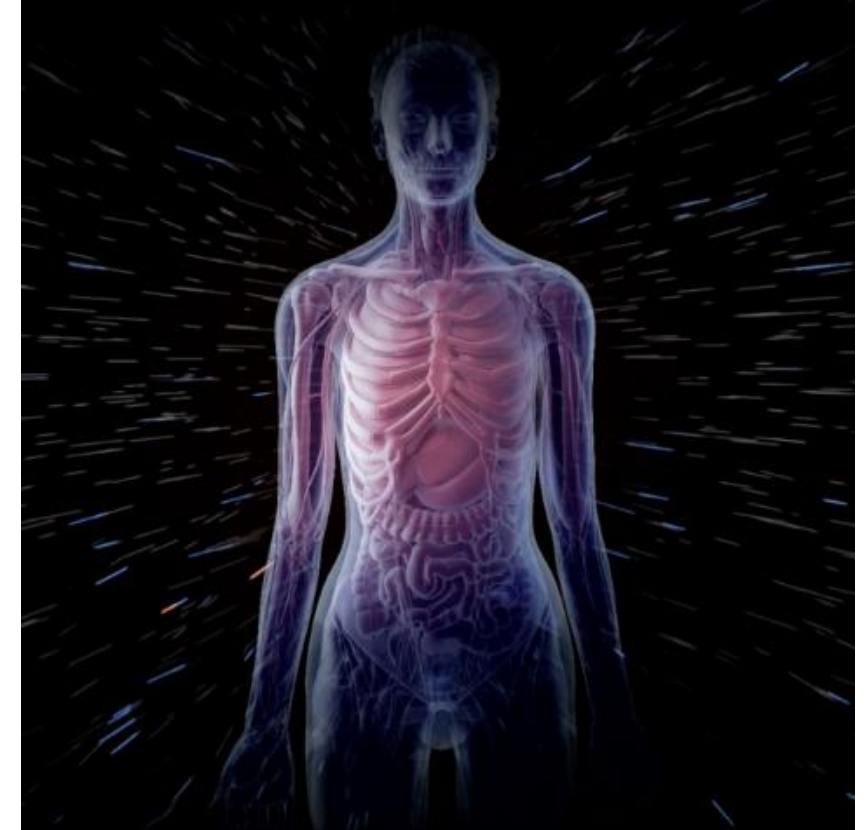


- Galactic Cosmic Ray Simulator (GCRsim) Beam Overview
- Prior Verification Results with Digimouse and Digirat
- Digipig
- Geant4 Simulation of GCRsim Beam in Digipig
- Geant4 Simulation Cross Species Comparison
- Summary and Conclusions

GCRsim Beam Overview



- Space radiation poses multiple important health risks for astronauts
- Risk of cancer, cardiovascular disease, and damage to Central Nervous System
- For long duration mission beyond low Earth orbit (LEO) risks mainly arise from galactic cosmic rays (GCR)
- Ground-based experiments will help to mitigate risks and reduce uncertainties



GCRsim Beam Overview

Background



- Previous ground-based radiation studies were done with single mono-energetic beams directly onto the biological sample
 - Helped with understanding underlying biological mechanisms
 - However, poor analog for the complete space environment
- To better represent the complex mixed field environment in space, the GCRsim was developed at the NASA Space Radiation Laboratory (NSRL)
- The NSRL was commissioned in 2003, while the GCRsim was commissioned to use in 2017
- The first PI-led studies with GCRsim were performed in 2018



NASA's NSRL facility in Brookhaven, NY

GCRsim Beam Overview

Objective



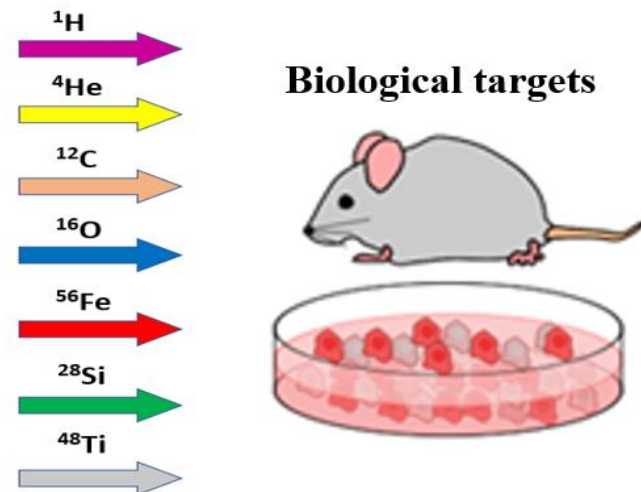
- Study health effects of GCR
- Simulate radiation environment as seen by astronauts in deep space missions
- Used in animal models and cell culture in a laboratory setting to simulate the target shielded tissue environment

GCRsim Beam Overview

Simulation Approach

- The GCRsim uses the local field approach
- Models are used to assess the radiation environment exposed to astronauts
- Multiple beams are selected to collectively represent the shielded tissue radiation environment
- Biological targets are sequentially irradiated with the selected beams

Beams selected directly to represent the shielded tissue environment

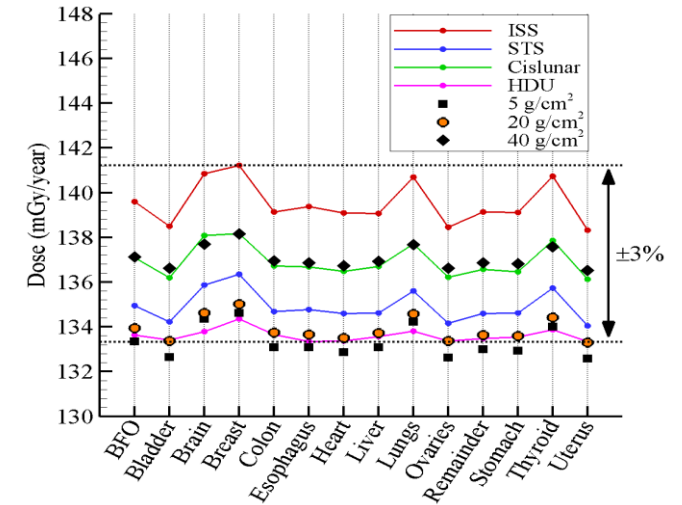


GCRsim Beam Overview

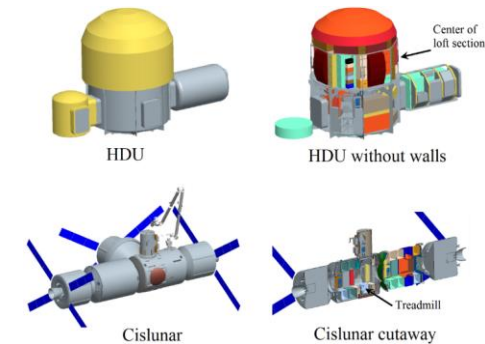
Reference Field



- Shielded tissue field in space depends on several factors
 - Tissue location
 - Shield design
 - Solar activity
- A single reference field was defined to approximate deep space environment
 - Variation from these factors is smaller than uncertainty associated with trying to represent GCR at an accelerator



Female tissue dose behind various shielding configurations [Slaba 2016]

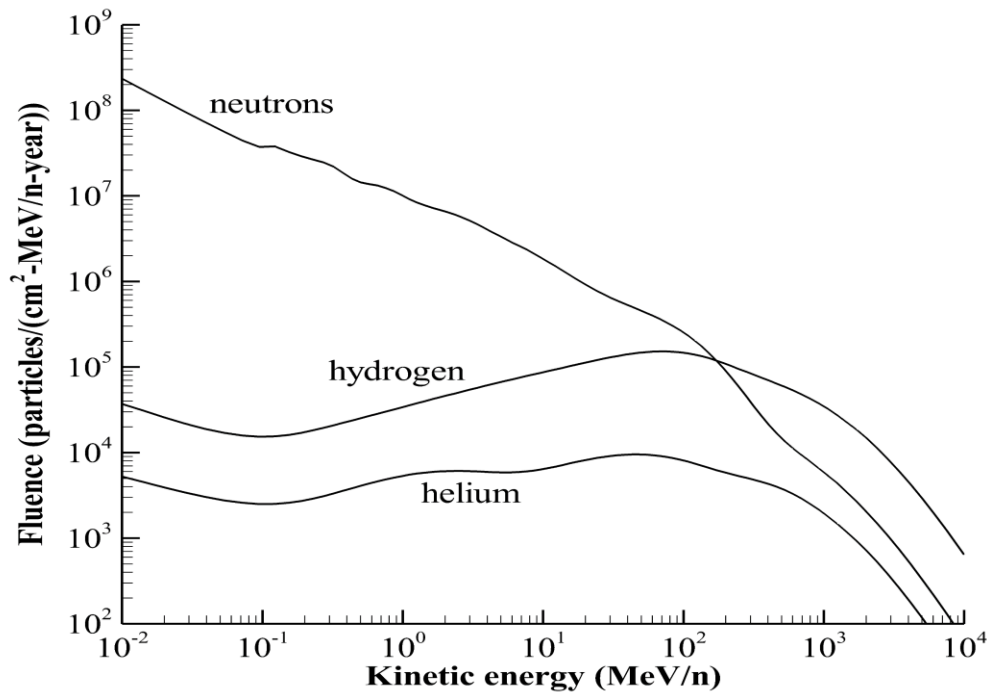


Different shield designs [Slaba 2016]

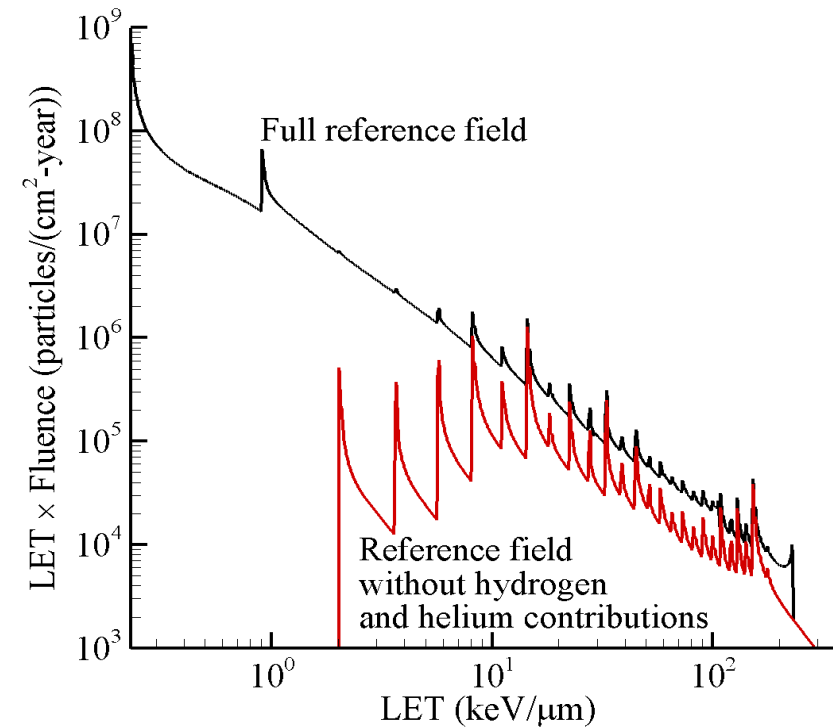
GCRsim Beam Overview

Reference Field

- Female BFO (blood forming organ) was chosen behind 20 g/cm² spherical aluminum shielding during solar minimum



Reference field energy spectra for neutrons, hydrogen, and helium [Slaba 2016]



Differential LET spectra of reference field with and without contributions from hydrogen and helium [Slaba 2016]

GCRsim Beam Overview

GCRsim Beam Definition at NASA

- The GCRsim at NSRL is designed to deliver deep space, shielded tissue environment to biological targets in a laboratory setting
- 33 mono-energetic beams of varying energies with ion species consisting of H, He, C, O, Fe, Si and Ti
- Sequential beam delivery reproducing the space environment over the full range of LET

Ion	Energy (MeV/n)	Range (cm)	LET (keV/μm)	Dose (mGy)
¹ H	100	<i>Polyethylene degrader to</i>		
¹ H	150	15.9	0.54	35.0
¹ H	250	38.1	0.39	68.9
¹ H	1000	326.6	0.22	123.6
⁴ He	100	<i>Polyethylene degrader to</i>		
⁴ He	150	16.0	2.17	7.5
⁴ He	250	38.3	1.56	16.4
⁴ He	1000	327.8	0.88	24.9
¹² C	1000	110.1	7.95	11.7
¹⁶ O	350	17.0	20.8	15.4
²⁸ Si	600	22.7	50.2	8.1
⁴⁸ Ti	1000	32.5	109.5	4.5
⁵⁶ Fe	600	13.1	175.1	4.1
Total				500.0

Ion	Energy (MeV/n)	Range (cm)	LET (keV/μm)	Dose (mGy)
¹ H	20.0	0.43	2.59	30.4
¹ H	23.3	0.56	2.29	6.7
¹ H	27.2	0.75	2.02	7.4
¹ H	31.7	0.98	1.79	8.0
¹ H	37.0	1.30	1.58	8.7
¹ H	43.2	1.72	1.39	9.3
¹ H	50.3	2.26	1.23	10.0
¹ H	58.7	2.99	1.09	10.6
¹ H	68.5	3.95	0.97	11.1
¹ H	79.9	5.20	0.86	11.2
¹ H	100.0	7.76	0.73	27.2

Ion	Energy (MeV/n)	Range (cm)	LET (keV/μm)	Dose (mGy)
⁴ He	20.0	0.43	10.34	11.0
⁴ He	23.3	0.57	9.14	2.1
⁴ He	27.2	0.75	8.06	2.2
⁴ He	31.7	0.99	7.12	2.3
⁴ He	37.0	1.31	6.29	2.5
⁴ He	43.2	1.73	5.56	2.6
⁴ He	50.3	2.28	4.92	2.7
⁴ He	58.7	3.01	4.36	2.7
⁴ He	68.5	3.97	3.86	2.7
⁴ He	79.9	5.23	3.43	2.7
⁴ He	100.0	7.81	2.90	6.1

GCRsim beam definition at NASA
[Simonsen 2020]

Previous Verification Results

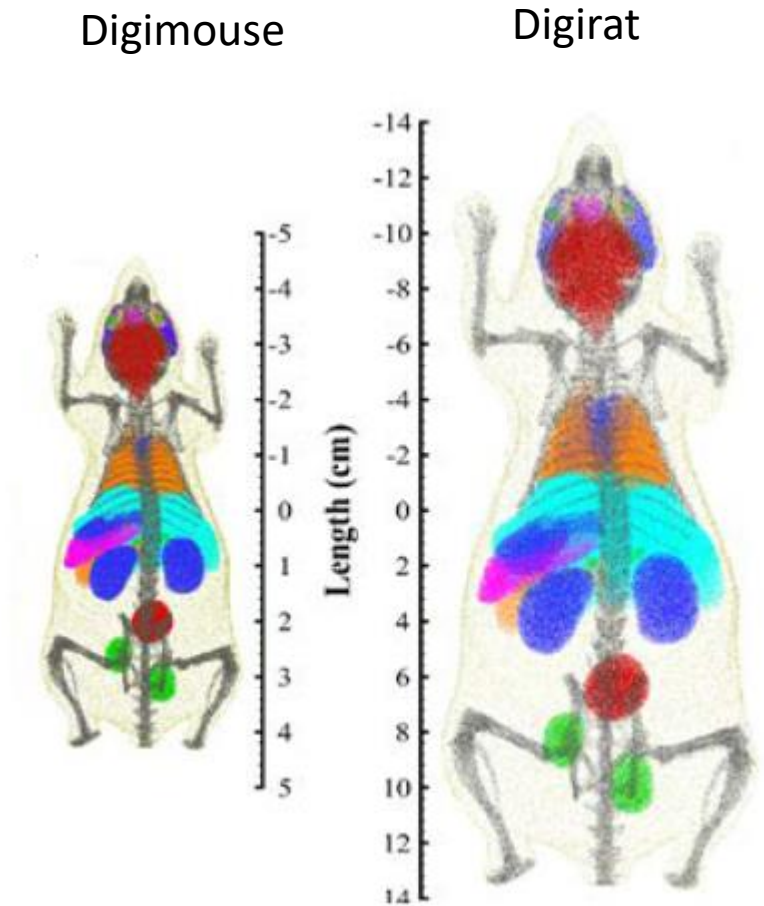


- The GCRsim is designed to be used for animals such as mice and rats to represent internal radiation environment seen at critical organ locations within the human body
- Radiation transport studies using phantom mouse and rat models have been previously completed to ensure that the GCRsim beams can provide a homogeneous dose distribution within the animal's internal organs
- In these transport studies the Geant4 Monte Carlo code was used to simulate the GCRsim in phantom models of mouse (Digimouse) and rat (Digirat)

Previous Verification Results

Digimouse and Digirat

- Digimouse is a 3D mouse atlas developed at the University of Southern California
 - Based on CT and cryosection images of a 28 g male mouse
 - Voxel dimension of 0.1 mm
 - Each voxel identifies a tissue or organ
 - Total of 21 segmented tissues/organs
 - Voxel dimensions: 208 x 380 x 992
- Digirat is an augmented model of Digimouse
 - All voxels scaled by a factor of 3.15
 - Total body mass of 754 g

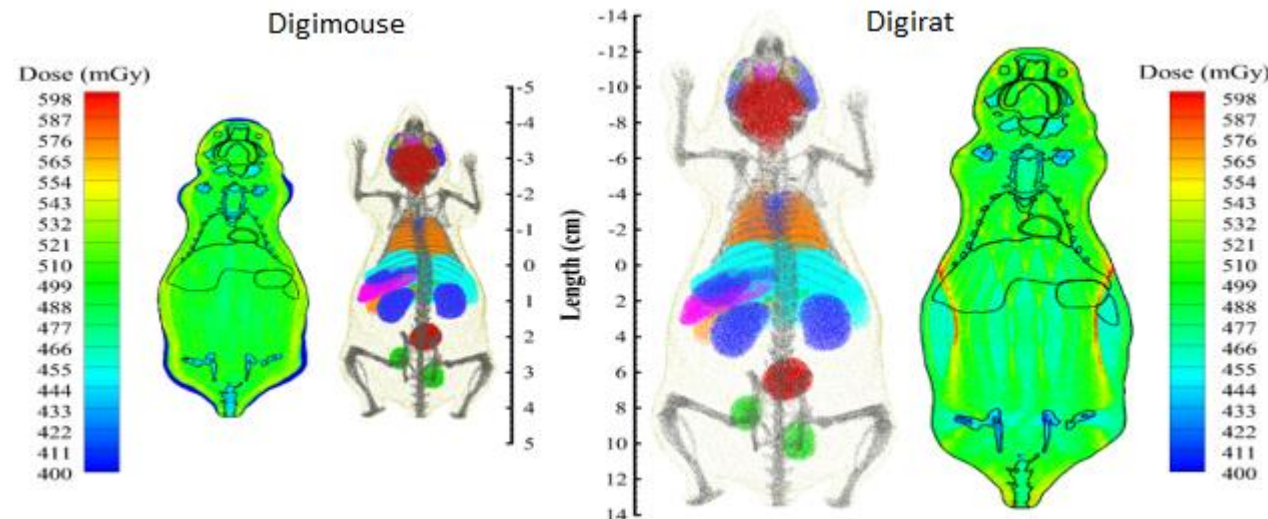


Digital models of rodent phantoms

Previous Verification Results

Dose in Tissues of Interest in Digimouse and Digirat

- Uniform dose across all tissues for both models
 - 95 % of voxel doses within 7% of average dose for Digimouse
 - 95 % of voxel doses within 10 % of average dose for Digirat
- Relatively good agreement with GCRsim beam dose of 500 mGy
 - Digimouse average Organ Dose: 500.7 mGy
 - Digirat average organ Dose: 490.7 mGy

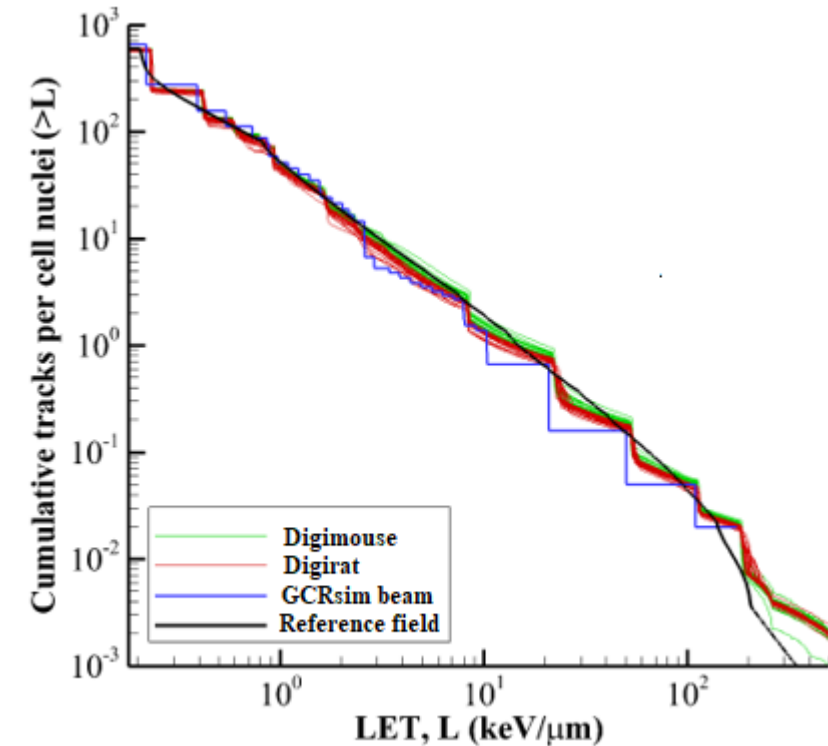


Dose distribution within Digimouse (left) and Digirat (right) [Simonsen 2020]

Previous Verification Results

Fluence Spectra as a Function of LET in Tissues of Interest

- Uniformity of spectra across all tissues
- Relatively good agreement with reference field
- The cumulative fluence at lower LETs is within ~2 % of the reference field
- The fluence can differ by ~40 % from the reference field at LETs above 200 keV/um when the fluence is very low

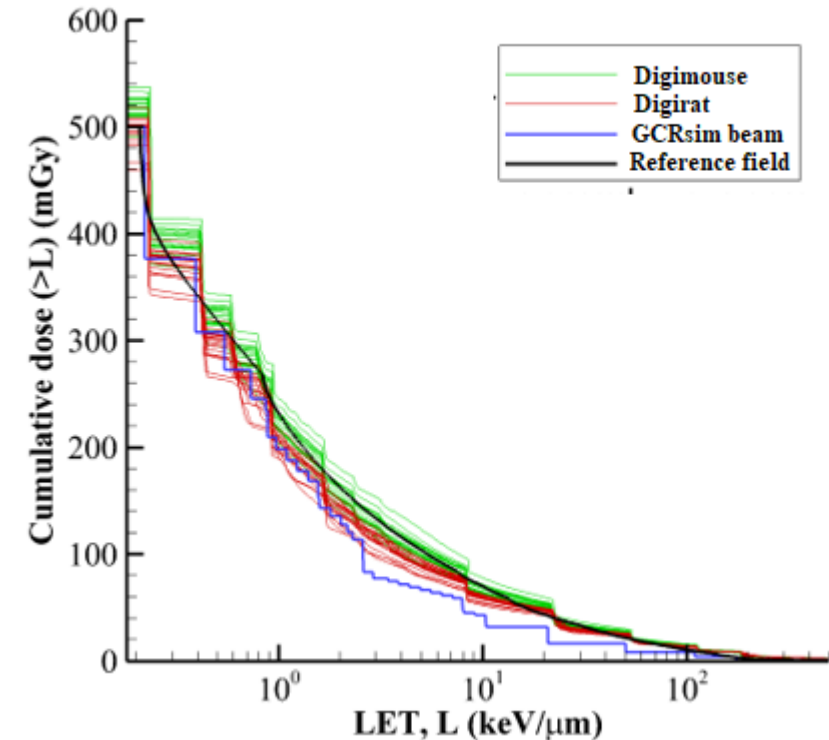


Cumulative fluence as a function of LET comparing simulated environments within Digimouse and Digirat tissues to the reference field and GCRsim beam exposure [Simonsen 2020]

Previous Verification Results

Dose Spectra as a Function of LET in Tissues of Interest

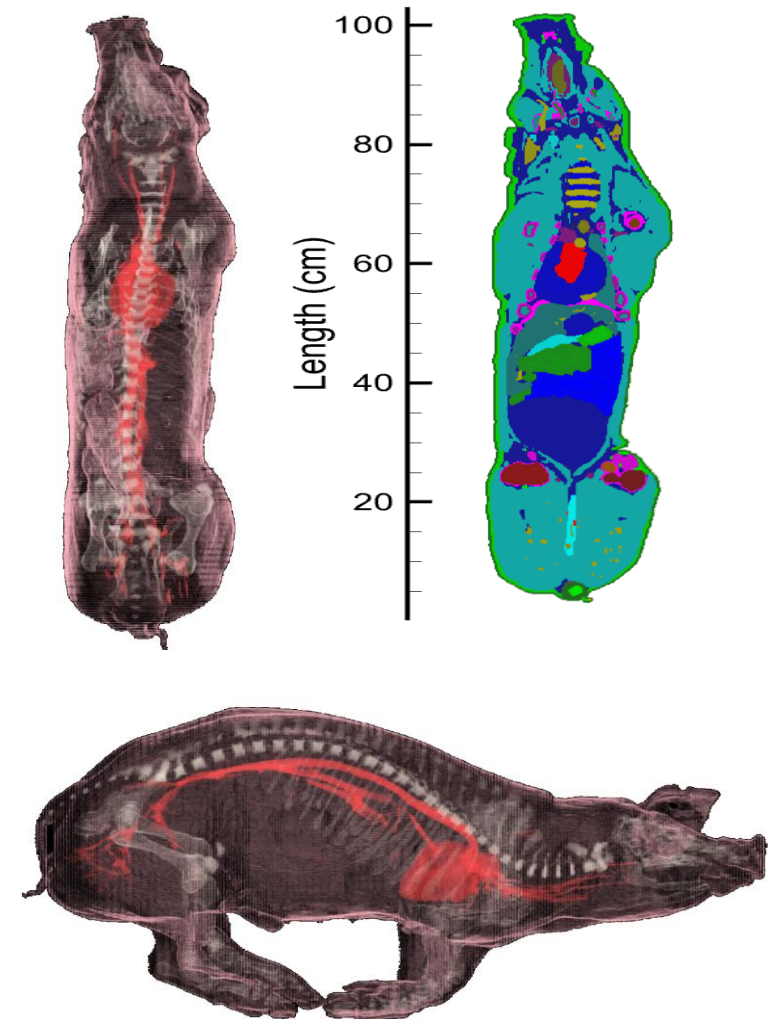
- Uniformity of spectra across all tissues
- Relatively good agreement with reference field
- The cumulative dose is within ~10 % of the reference field for most tissues at lower LETs



Cumulative dose as a function of LET comparing simulated environments within Digimouse and Digirat tissues to the reference field and GCRsim beam exposure [Simonsen 2020]

Digipig

- Digipig is a 3D anatomical model of a male mini pig
 - Developed by IT'IS foundation (Switzerland)
 - Created from magnetic resonance or cryosection image data of a 35 kg male domestic pig
 - 103 segmented tissues
 - Voxel dimensions: 490 x 1030 X 220
 - Voxel size of 1 mm

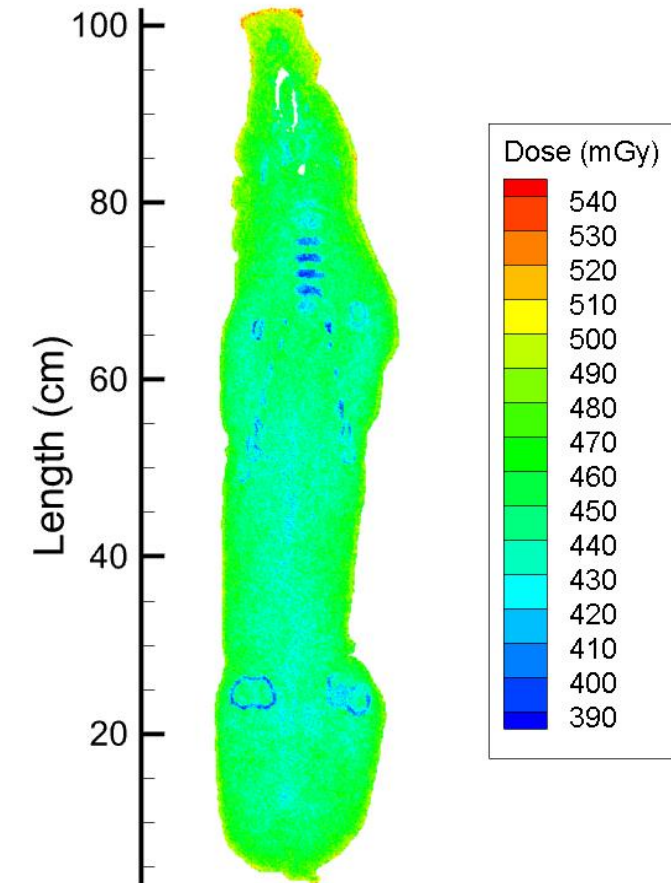


Cross sections of Digipig with tissue segmentation

Geant4 simulation of GCRsim beam in Digipig

Dose in Tissues of Interest

- Uniform dose across all tissues
 - 95 % of voxel doses within 8.2 % of average dose for Digipig
- Tissue dose comparison with the GCR beam of 500 mGy:
 - Average tissue dose = 446.2 mGy
 - Relatively good agreement with the GCR beam
 - However significantly lower agreement than Digimouse and Digirat



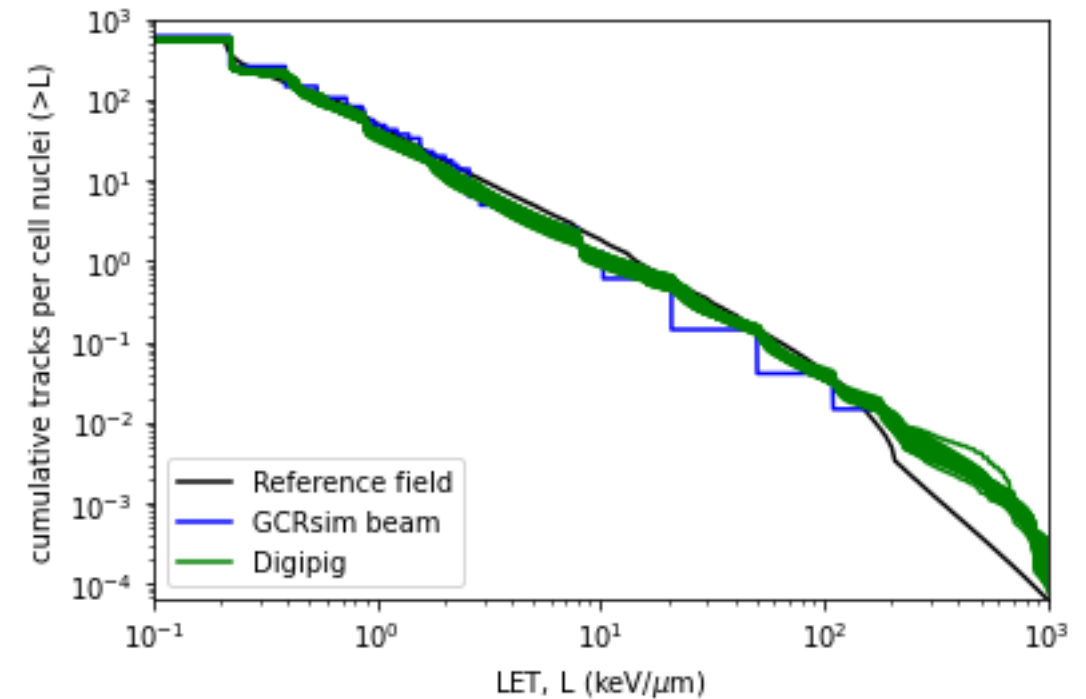
Dose distribution in Digipig from Geant4 simulation of GCRsim

Geant4 simulation of GCRsim beam in Digipig



Fluence Spectra as a Function of LET in Tissues of Interest

- Uniformity of spectra across all tissues
- Relatively good agreement with reference field
- The cumulative fluence at lower LETs is within ~4 % of the reference field
- The fluence can differ by ~50 % from the reference field at LETs above 200 keV/ μm when the fluence is very low

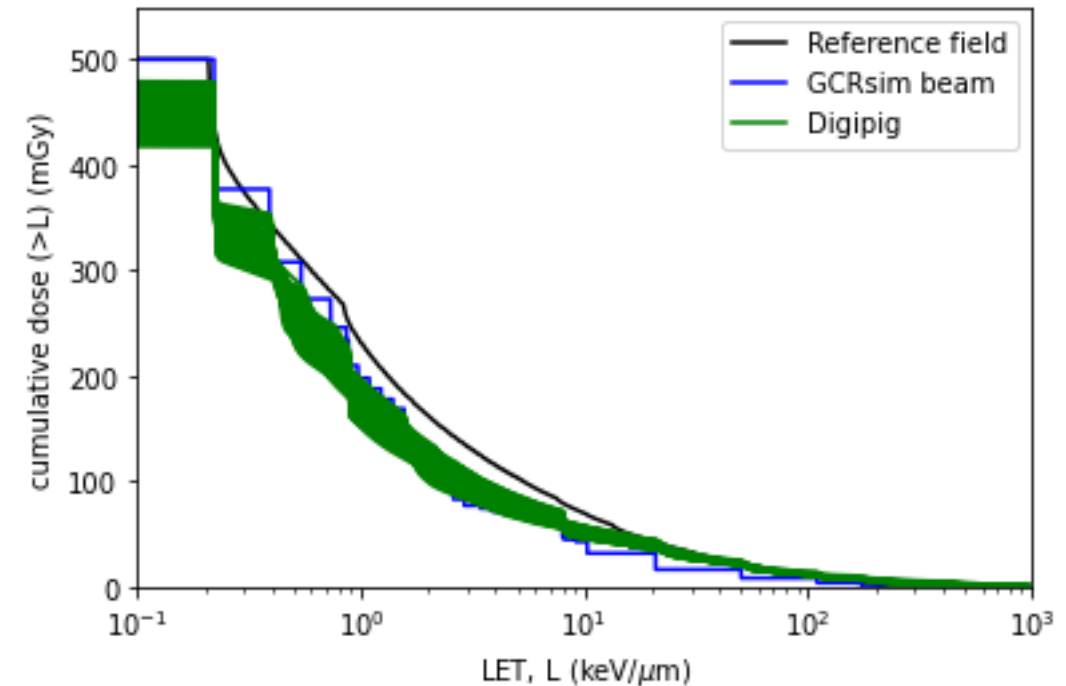


Cumulative fluence as a function of LET comparing simulated environments within Digipig tissues to the reference field and GCRsim beam exposure

Geant4 simulation of GCRsim beam in Digipig

Dose Spectra as a Function of LET in Tissues of Interest

- Uniformity of spectra across all tissues
- Somewhat good agreement with reference field
- At lower LETs the cumulative dose can differ by approximately 15 % and by approximately 100-200 % for LETs around 50-150 keV/ μm

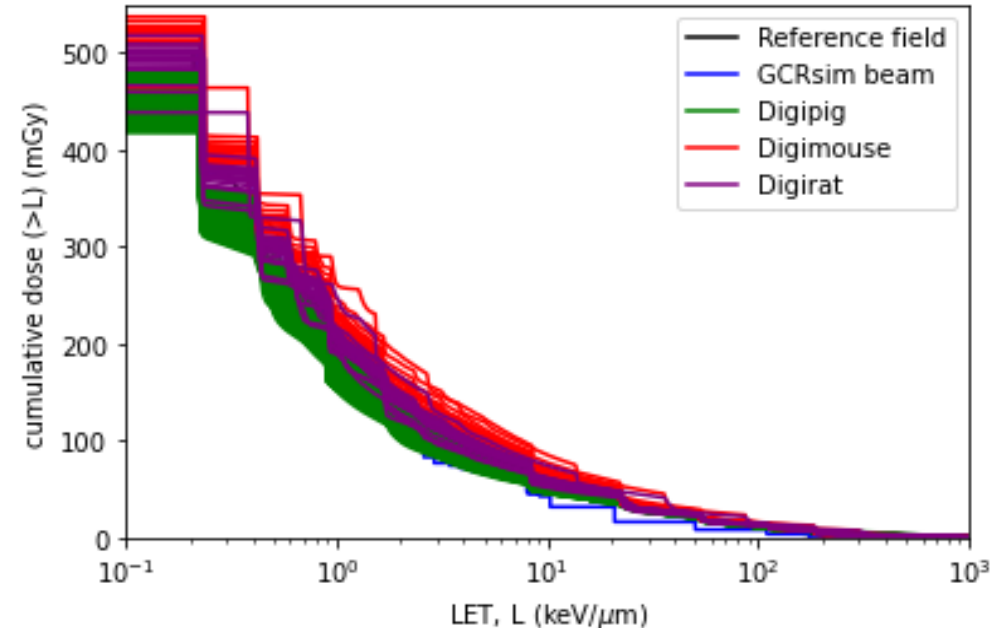
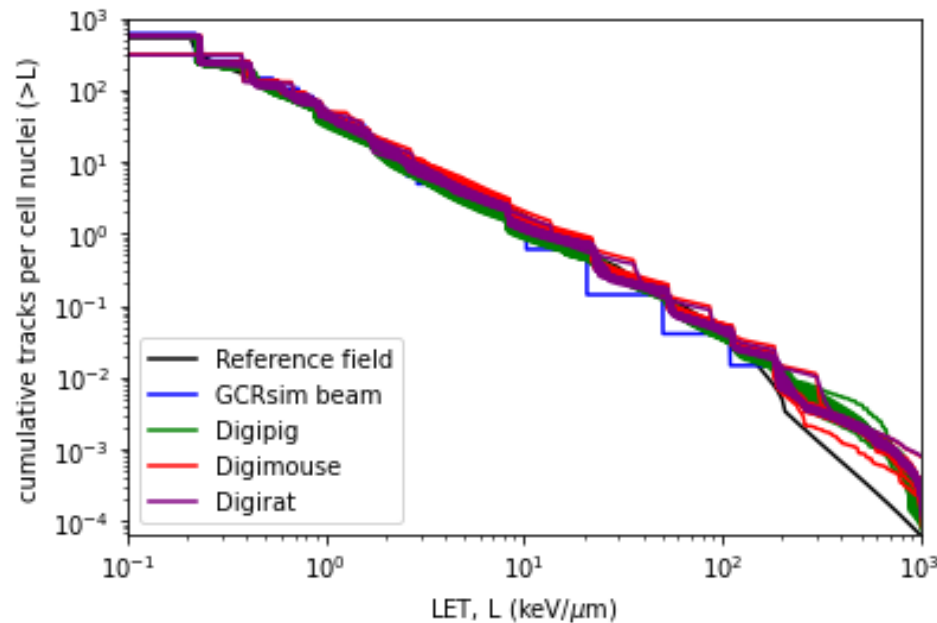


Cumulative dose as a function of LET comparing simulated environments within Digipig tissues to the reference field and GCRsim beam exposure

Geant4 Simulation Cross Species Comparison



- The fluence spectra for all animal models match relatively well with the reference field across all LETs
- For dose spectra, however, Digipig consistently undermatches the cumulative dose for all tissues as compared to Digimouse and Digirat



Comparison of the cumulative fluence (left) and cumulative dose as function of LET (right) in the different animal models

Geant4 Simulation Cross Species Comparison

Comparison of Tissue Dose to Major Radiosensitive Organs for GCR Beam of 500 mGy

Organ	Organ Dose (mGy)		
	Digimouse	Digirat	Digipig
Skin	525.1	499.0	486.7
Brain	532.8	492.3	460.1
Eye	532.4	497.0	474.7
Heart	517.4	487.0	444.4
Bladder	519.0	486.1	440.9
Testis	528.3	491.1	468.1
Stomach	519.4	487.3	446.1
Spleen	530.7	493.0	446.8
Pancreas	520.5	488.2	439.9
Liver	519.2	487.6	446.3
Kidneys	519.8	487.8	451.3
Adrenal glands	512.5	483.7	450
Lung	515.6	485.4	444
Skeleton	470.2	442.9	406.7
Mean soft tissue dose	523.5 ± 7.3	490.4 ± 19.3	454.4 ± 14.1

Summary and Conclusions



- We reviewed past verification of GCR beam with Digimouse and Digirat
- We introduced Digipig and showed verification results with GCRsim beam
 - Showed uniform dose distribution across all voxels and tissues
 - Average tissue dose was around 11 % lower than the GCR beam dose
 - The fluence spectra matched well with the reference field and was comparable to Digimouse and Digirat results
 - In contrast to the Digmouse and Digirat results, which matched well with the reference field, the cumulative dose spectra for Digipig was significantly lower than the reference field, especially at lower fluences
- Next Steps
 - Publish results for the manuscript
 - Direct application of GCRsim beam for minipigs may be valid
 - Errors introduced by increased mass may not be large enough to justify changing the GCRsim beam definition
 - Would need to account for more detailed experimental factors
 - Interact with PIs to determine requirements and make adjustments if needed

References



- [Simonsen 2020] Simonsen, L. C., T. C. Slaba, P. Guida, and A. Rusek. "NASA's first ground-based galactic cosmic ray simulator: Enabling a new era in space radiobiology research." *PLoS Biology* 18, no. 5 (2020): e3000669.
- [Slaba 2016] Slaba, T. C., S. R. Blattnig, J. W. Norbury, A. Rusek, and C. La Tessa. "Reference field specification and preliminary beam selection strategy for accelerator-based GCR simulation." *Life Sciences in Space Research* 8 (2016): 52-67.